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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,597	04/15/2004	Stephen J. Pandol	034044.021CIP1	7147

53498 7590 10/07/2009

Suzannah K. Sundby (UC)
SMITH, GAMBRELL & RUSSELL, LLP
1130 Connecticut Avenue, NW
Suite 1130
WASHINGTON, DC 20036

EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
10/07/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SSUNDBY@SGRLAW.COM
dcdocketing@sgrlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/824,597	PANDOL ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 37-57 are presented for examination.

Applicant is notified that the finality of the previous Office Action dated 11/13/2008 is hereby withdrawn. The after-final amendment filed 4/13/2009 has been entered into the record and prosecution of the present application has been reopened.

Applicant's arguments filed 4/13/2009 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Objection

There appears to be no claim numbered 56. Applicant recites claim 55 and then claim 57. Applicant's amendments are not in compliance with 37 CFR 1.121. A new claim set properly numbered is required.

Priority

This application is a continuation-in-part of Application No. 10/260.609 now U.S. 6,953,786.

The disclosure of the prior-filed applications, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. All claims are not adequately supported or enabled by the prior-filed applications for a method of treating or inhibiting pancreatitis or pancreatic cancer in a subject which comprises administering a therapeutically effective amount of rottlerin.

It is noted that Applicant is not entitled to the priority date in these application for all claims in the instant claim set because the information contained within the previous referred filings does not support the granting of an earlier filing date. Specifically, the prior filing of the continuation-in-part and

continuations does not support the written description and enablement requirement for a method for the treatment of gastrointestinal tumors. **All claims are given a priority date of April 15, 2004 for prior art purposes.**

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates a method of treating or inhibiting pancreatitis or pancreatic cancer in a subject which comprises administering a therapeutically effective amount of rottlerin.

Inhibition is defined as the action of prohibiting (definition from www.freedictionary.com). Prohibiting is defined as prevention (definition from www.freedictionary.com). Therefore, Applicant's invention is drawn to the prevention of pancreatic cancer.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

2. The breadth of the claims

The claims are extremely broad insofar as they disclose the general treatment and prevention of pancreatic cancer, regardless of the underlying primary cause of such cancer.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to *prevent* pancreatic cancer, particularly in humans. Further, there is no working example whereby animals or humans predisposed to

developing pancreatic cancer are prevented from developing such a cancer simply by administration of the claimed compound.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed compounds could be predictably used as a treatment or prevention of pancreatic cancer as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

The prevention of cancer is entirely unpredictable due the diverse environmental, genetic, and biological causes of cancer. Further still, there is limited evidence in the prior art that compounds useful in treating cancer are also effective in preventing the same cancer they treat.

Determining if any particular claimed compound would *prevent* pancreatic cancer would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claims the subject matter which Applicant regards as the invention. Claim 37 recites the administration of a "therapeutically effective amount" of rottlerin. This limitation is indefinite because it is unclear what the amount being administered is effective. The specification provides no guidance or definition of a "therapeutically effective amount" of rottlerin. The phrase "therapeutically effective amount" being administered has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner

to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37, 44, 46-48, 55 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yazbeck et al. (Gastroenterology, 124, A103, 2003) in view of King (U.S. 2002/0048582).

Yazbeck et al.. teaches that the protein kinase C inhibitor rottlerin greatly stimulates apoptosis in pancreatic cancer cells (page 3).

Yazbeck et al. is silent on the treatment in a subject.

King et al. teach that rottlerin is known to be treatment for modulation of angiogenesis and tumor metastasis in a subject (claims 1 and 3). The compounds of the instant invention are administered at an effective amount (paragraph [0114]).

It would have been prima facie obivious to one having ordinary skill in the art to administer roterlin to a patient having pancreatic cancer because Yazbek et al teach that rottlerin stimulates programmed cell death in pancreatic cancer cells and one would have a reasonable expectation of success because King et al teach that rottlerin is active in vivo. One would have been motivated to do so given that rottlerin has been taught to be effective in a subject for modulation of angiogenesis and tumor metastasis.

Claims 40, 45, 49-50 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yazbeck et al. (Gastroenterology, 124, A103, 2003)in view of King (U.S. 2002/0048582) as applied to claims 37, 44, 46-48, 55 and 57 above, and further in view of Mouria (Int. J. Cancer, 98, 761-769, 2002; of record).

The combination of Yazbeck et al. in view of King et al. is set forth supra. The combination differs by not administering genistein.

Mouria et al. teach that the effects of genistein was investigated on pancreatic carcinoma cells (abstract). Inhibitory effects of genistein on the development of metastatic lesions and the growth of the primary tumor in the same model of pancreatic cancer was observed (bridging pages 763-764). Genistein is also known to stimulate both apoptosis and caspase activation (page 765). Finally, the authors conclude that the genistein causes apoptosis in pancreatic cancer cells (page 766, column 2, paragraph 4).

One of ordinary skill would have found it prima facie obvious to administer rottlerin and genistein for the treatment of pancreatic cancer with a reasonable expectation of success.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to add the genestin of Mouria with the rotterlin as combined supra because the combination of the agents, each known for the treatment of pancreatic cancer would have expected to display additive if not superadditive results.

Claims 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yazbeck et al. (Gastroenterology, 124, A103, 2003) in view of King (U.S. 2002/0048582) as applied to claims 37, 44, 46-48, 55 and 57 above, and further in view of Shaw et al. (U.S. 2004/0259942).

The combination of Yazbeck et al. in view of King et al. is set forth supra. The combination differs by not administering diphenylene iodonium.

Shaw et al. teaches that diphenylene iodonium is taught for the treatment of pancreatic adenocarcinoma (paragraphs [0008] and [0041]).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to add the diphenylene iodonium of Shaw et al. with the rotterlin as combined supra because the combination of the agents, each known for the treatment of pancreatic cancer would have expected to display additive if not superadditive results.

Claims 42-43 and 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yazbeck et al. (Gastroenterology, 124, A103, 2003) in view of King (U.S. 2002/0048582) as applied to claims 37, 44, 46-48, 55 and 57 above, and further in view of Shaw et al. (U.S. 2004/0259942) and Detjen (Journal of Cell Science, 113, 3025-3035, 2000).

The combination of Yazbeck et al, in view of King et al. is set forth supra. The combination differs by not administering peptide delvaV1-1.

Mochly-Rosen et al. teaches the administration of peptide deltaV1-1 to tumor cells for the treatment of solid tumors (column 5). Further it is taught that deltaV1-1 can activate PKC (column 2).

Detjen teaches that activation of protein kinase C inhibits growth of pancreatic cancer cells (title and abstract).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to add the delta V1-1 of Mochly-Rosen et al. with the rotterlin as combined supra because delvaV1-1 is known to be administered to tumors and activates PKC which activation is known to inhibit growth of pancreatic cells.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645